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Remarks

Claims 63 and 104 have been amended and new claims 110-113 added herein. Support for the amendments lies in the original claims and specification as filed, and no new matter is added by virtue of these amendments. For example, support for new claims 110-113 lies, for example in original claims 28 and 29, and in the specification at page 18, lines 15-23, and Preparative Example 3 and Figure 3; support for the amendment to claim 104 lies in the original specification, for example, at page 15, line 21 through page 16, line 14; and support for the amendment to claim 63 lies, for example, in original claims 1, 13, 18, 22, 24.

Oath/Declaration

The Examiner has indicated that the Declaration is defective on the grounds that (i) it does not identify the mailing address of each inventor and (ii) it does not identify the U.S. provisional application to which priority is claimed. Applicants submit herewith an executed Declaration. It is believed the present submission is in compliance with 37 CFR 1.67(a). Reconsideration and withdrawal of the objection is respectfully requested.

Specification Objections

The specification was objected to as failing to provide proper antecedent basis for the claimed subject matter. The Examiner indicated the specification does not appear to provide antecedent basis for the language "specific predefined proteins" as recited in claims 63 and 84.

Applicants submit the phrase "specific predefined ligand" is supported in the original claims as filed (see e.g., original claim 27). Applicants further submit the use of "protein" in lieu of ligand is clear to one skilled in the art that a protein is a subset of types of ligand which may bind a receptor (see e.g., original claim 30). One skilled in the art would immediately recognize the metes and bound of the phrase, thus, such phrase is not indefinite nor unclear. Reconsideration and withdrawal of the rejection is requested.

Rejections under 35 U.S.C. § 112

Claims 32, 52, 62-69, 84-85, 88-89 and 104-107 were rejected under 35 USC §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner objected to the recitation of "specific predefined proteins" in claims 63 and 84 as indefinite and lacking antecedent support in the specification. Applicants respectfully traverse the rejection.

As discussed above, Applicants submit the phrase "specific predefined ligand" is supported in the original claims as filed (see e.g., original claim 27). Applicants further submit the use of "protein" in lieu of ligand is clear to one skilled in the art that a protein is a subset of types of ligand which may bind a receptor (see e.g., original claim 30). One skilled in the art would immediately recognize the metes and bound of the phrase, thus, such phrase is not indefinite nor unclear. Reconsideration and withdrawal of the rejection is requested.

The Examiner objected to the recitation of "solid phase matrices" in claim 63 as lacking antecedent basis and as indefinite. The rejection is traversed.

Applicants submit initial reference to "a first and second solid phase matrix" is in proper antecedent form. Initial introduction of the "first and second solid phase matrix" clearly provides antecedent basis for the later reference to "the first and second solid phase matrices." Since initial introduction clearly provides a plurality of matrices (rather than a single matrix) as being present, later reference to the matrices as plural together should not be indefinite nor unclear. Applicants thus submit the recitation of "solid phase matrices" does have proper antecedent basis, and clearly references the prior recitation of "a first and second solid phase matrix."

However, solely in an effort to advance prosecution, and address the concern of the Examiner, Claim 63 has been amended such that the recitation now recites "a first and a second matrix." Applicants submit the present amendment in no way changes the meaning, interpretation, scope or limitations of the claim. Withdrawal of the objection is respectfully requested.

The Examiner objected to the recitation of "each solid phase matrix comprises a plurality of particles" in claims 63 and 84 as indefinite. The Examiner asserts whether/how a bead comprises a "plurality of particles" is not clear. The rejections are traversed.

Applicants submit that those of ordinary skill in the art would understand the claim language to refer to a collection of solid phase matrices, each of which is made up of a collection of particles. Such forms of solid phase matrices are familiar to those of ordinary skill. The text excerpt cited and utilized by the examiner does refer to "a matrix" as "a bead". One of ordinary skill in the art would understand that a single bead can constitute a complete matrix. However, one of ordinary skill is also aware that a single solid phase can alternatively be comprised of a collection of beads. Indeed, the specification provides examples of various resins and other materials that are commonly utilized in solid phases comprised of a plurality of particles or beads. The present claims clearly specify that they relate only to those embodiments in which a single solid phase is comprised of a collection of particles. The language is both clear and definite. Reconsideration and withdrawal of the rejections is thus respectfully requested.

The Examiner objected to the recitation of "a first and second solid phase matrix contacting each other" in claim 63 as indefinite. The Examiner also objected to the recitation of "each solid phase matrix is in contact with at least one other solid phase matrix" in claim 84 as indefinite. The Examiner asserts whether/how a matrix of beads is in contact with another matrix of beads is not clear, and whether "contacting" or "in contact" requires a matrix to be stacked, layered, and/or adjoined is not clear. Additionally, the Examiner stated if stacked, layered, or adjoined, how a mixture can be present is not clear. The rejections are traversed.

The objected phrases are similar, and the Examiner references the identical recitation in the specification as supporting the assertion of lack of clarity. Thus, in the interest of brevity, the two objections will be addressed in conjunction. Applicants submit the objected phrases are clear and would readily be understood to one skilled in the art. Applicants submit the objected phrase, on its face alone comprises possibility of being "in contact" includes by stacked, layered, and/or adjoined possibilities as the examiner suggests. However, Applicants submit "in contact" also includes mixtures of particles comprising matrices. Applicants point out the present claims further include limitation "wherein the plurality of particles of the solid phase matrices are present as a mixture in the affinity binding composition;". Thus, in the entire claim context, particles of each of the matrices are present in a mixture in the claimed affinity binding composition. Applicants point out description of preparation of mixtures of matrices and affinity compositions as claimed are provided throughout the specification. For example, see Preparative Example B, and Example 1.

Reconsideration of the claimed subject matter in the entirety of claim context, and withdrawal of the rejections is thus respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 32, 52, 62-69, 84, 89 and 104 were rejected under 35 USC § 102(b) as being anticipated by Stausbøl-Grøn, et al., 391 *FEBS Letters* 71 (1996). This reference is referred to as Brian, et al., in the Office Action and will be referred to as "Brian" herein. Applicants note the rejection is identical to that set forth in prior Office Action mailed August 22, 2005.

Applicants submit that Brian teaches placing an immunobead in an immunotube containing a sample comprising phage and soluble proteins, removing the immunobead from the immunotube, washing the immunobead, and eluting phage that had bound to the immunobead. Brian also teaches use of an immunotube having a mixture of proteins attached thereto (MIX), and an immunotube having a mixture of proteins attached thereto as well as a specific protein of interest (MIX + LDH). The sample also contains MIX proteins in solution. Brian does not necessarily teach removal of two specific, predefined proteins from the sample. Rather, the teachings of Brian direct isolation of phage that are specific for one selected protein (exemplified as LDH).

As discussed in Applicants' prior response, there is no indication that any proteins bound to the immunobead during the incubation. Even if proteins did bind, washing the immunobead does not constitute any teaching of removing two specific, predefined proteins from the sample because it is entirely unclear which proteins, if any, may have bound. During the interview, the Examiner alluded to the possibility that antibodies displayed by the phage, which bound to the target proteins on the immunobead, could be considered to be "at least two specific, predefined proteins" such that removal of the phage bound to the beads constitutes removing at least two specific, predefined proteins from the sample. Applicants respectfully disagree.

First, Applicants respectfully submit that one of ordinary skill in the art would not consider removal of a phage to be removal of a "specific protein" as recited in the present claims. Furthermore, even if antibodies displayed by the phage could be considered to be a specific protein, Brian certainly does not teach that necessarily more than one specific protein is selected or removed from the sample, much less "at least two specific, predefined proteins." Brian does not indicate that phage that bound to the immunobeads did in fact display at least two different antibodies directed to the proteins bound to the beads. Brian simply states that he was able to preferentially enrich for

phage that bound to LDH and that after three rounds of selection, the results suggested non-significant binding against MIX proteins. (p. 73, right col., last paragraph). Thus the only evidence provided by Brian regarding antibodies displayed by the phage is that they bound to LDH. Brian does not say anything about antibodies that might bind to different proteins, neither suggest that more than one antibody was isolated that was directed to LDH. Thus, Applicants submit no teaching is provided in Brian for removal of phage from the immunotube which constitutes removal of at least two specific, predefined proteins as recited in the instant claims.

During the interview discussion, the Examiner acknowledged Brian does not teach recovery of a modified sample. Rather, Brian teaches recovery of phage that bound to the immunobeads. During the interview discussion, it was agreed that Applicants would specifically refer to this distinction between Brian and the claimed invention in the instant Office Action Response. Applicants note the Examiner's comments and response did not acknowledge this distinction and deficiency of Brian.

The Examiner asserts that Brian teaches that the removing step comprises "contacting the sample with an affinity binding composition ...comprising a first and second solid phase matrix contacting each other, wherein each solid phase comprises a plurality of particles." The Examiner indicated that the first solid phase matrix is the immunobeads and the second solid phase matrix is the immunotube. As discussed in Applicants' prior response and during the interview, the Examiner acknowledged that the immunotube is not a plurality of particles, and it was further pointed out that since the immunobeads all have the same mixture of proteins attached thereto, i.e., MIX+LDH or FM55p proteins, the immunobeads are not first and second solid phase matrices. Furthermore, even if the immunobeads comprising MIX+LDH and the immunotube could be considered as providing a teaching of a first and second solid phase matrices, they are not present as a mixture in the affinity binding composition provided.

Applicants respectfully request the Examiner carefully consider the distinctions outlined herein demonstrating the differences of the teaching of Brian and the presently claimed invention. The Examiner asserted in the prior response that Applicants' comments relied on a particular set of experiments performed by Brian, and does not appear to give deference to the broader analytical framework established by Brian et al. Applicants respectfully disagree with the Examiner's position, and point out that an effective anticipatory reference must necessarily teach each and every limitation of a claimed invention. Thus, a broad interpretation of an analytical framework potentially extrapolated from what may (or may not) be actually taught by Brian is not a proper use

of the specific teaching of Brian as an anticipatory reference. Still further, even assuming arguendo, that the analysis of differential gene expression as a broader framework of the teaching of Brian were proper, Applicants submit such extrapolation does not supply the missing features to Brian that would be required to provide an effective anticipating reference.

In summary, Brian does not provide a teaching of a method of removing at least two specific predefined proteins from a sample; nor does Brian provide a method for producing and recovering a modified sample. Still further, no teaching of a first and second solid phase matrix, each comprising a plurality of particles present as a mixture in the affinity binding composition is provided. As such, Brian cannot be a valid anticipatory reference. Reconsideration and withdrawal of the rejection is thus respectfully requested.

Claims 32, 52, 62-69, 84, 88-89 and 104 were rejected under 35 USC § 102(e) as being anticipated by Payan (U.S. Patent 6,455,263). The Examiner asserts Payan teaches a method for separating proteins from a sample that contains proteins comprising the steps: removing at least two specific predefined proteins from a sample that contains the at least two specific predefined proteins, thereby producing a modified sample containing a plurality of proteins, recovering the modified sample, wherein the removing step comprises contacting the sample with an affinity binding composition comprising a first and second solid phase matrix contacting each other, wherein each solid phase matrix comprises a plurality of particles, and wherein the particles are present as a mixture. Applicants respectfully traverse the rejection.

Applicants respectfully submit Payan provides a teaching of utilizing FACS for screening library molecules. The teaching of Payan directs one to attach a library of compounds to be assessed to a solid support, followed by assessment of binding of fluorescent agents to the library to determine the presence of a compound having a desired characteristic. The teaching of Payan does not extend to the methods of Applicants claimed invention.

An effective anticipatory reference must provide a teaching necessarily containing each and every limitation of a claimed invention. Payan does not teach use of a method for removal of two specific proteins from a sample. In fact, Payan does not teach recovery of a modified sample from an affinity binding composition. Further, Payan does not necessarily teach removing at least two specific proteins from a sample. Still further, Payan does not teach a first and second solid phase matrix comprising a first receptor and a second receptor, respectively, which are capable of binding

specific proteins. As such, Payan cannot provide an anticipatory teaching to the presently claimed invention. Withdrawal of the rejection is thus respectfully requested.

Rejections under 35 U.S.C. § 103(a)

Claims 32, 52, 62-69, 84-85, 88-89 and 104-107 were rejected under 35 USC § 103(a) as being unpatentable over Davies (U.S. Patent 6,696,304) in view of Payan (U.S. Patent 6,455,263). The Examiner stated that it would have been obvious to perform the method of Davies with added procedural steps of producing and recovering a modified sample because Payan discovered that producing and recovering a modified sample using FACS allows for subsequent analysis, treatment, and/or characterization. The rejection is traversed.

Applicants respectfully disagree with the Examiner's assertion. Applicants respectfully point out the method of Davies provides for preparation of protein-immobilized microparticles, and methods of detecting and calibrating the amount of protein bound to a solid support. Applicants submit the teaching of Davies does not provide any teaching of preparation of a mixture of particles comprising different receptors, much less a mixture of solid phase matrices comprising a plurality of particles. The teaching of Davies extends no further than methods for assembling a protein to a solid support, and effectively determining the amount of resulting bound protein to the support.

Applicants respectfully submit that even had motivation to combine Davies and Payan existed, which it does not, replacing the method of Davies with the method of Payan would not render the claimed invention obvious. As discussed above, Payan does not teach use of a method for removal of two specific proteins from a sample. In fact, Payan does not teach recovery of a modified sample from an affinity binding composition. Payan does not necessarily teach removing at least two specific proteins from a sample. Nor does Payan teach a first and second solid phase matrix comprising a first receptor and a second receptor, respectively, which are capable of binding specific proteins.

In summary, there is no motivation to combine the teachings of Davies and Payan, and even if such a motivation existed, the resulting combination still would not teach each of the features of the claimed invention. Applicants therefore submit that the instant claims are not obvious for each of the foregoing reasons. Withdrawal of the rejection is respectfully requested.

In conclusion, in view of the remarks presented herein, none of the cited art anticipates any of the claims pending in the instant application nor renders them obvious. Applicants therefore respectfully submit that the present case is in condition for allowance. Early Notice to that effect is respectfully requested.

Applicant's note the prior Office Action was mailed to Customer Number 24280, and respectfully request all future correspondence be directed to Customer Number 022878, according to the Request for Change in Correspondence Address, which was filed and entered 08 July, 2005, a copy of which is enclosed.

If, at any time, it appears that a phone discussion would be helpful, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5000 or (617) 248-4831 (direct dial).

This response is being filed via facsimile with a petition and request for a three month extension of time, as well as the requisite fee payment. It is believed no additional fees are due in connection with this submission. However, in the event any additional fees or extensions are due, please consider this a petition therefore, and please charge any fees associated with this filing, or apply any credits, to Deposit Account No. 50-1078.

Respectfully submitted,



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